Agency for Healthcare Research and Quality
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NATIONAL GUIDELINE CLEARINGHOUSE

General

Guideline Title

Congress of Neurological Surgeons systematic review and evidence-based guidelines on the role of radiosurgery and radiation therapy in the management of patients with vestibular schwannomas.

Bibliographic Source(s)

Germano IM, Sheehan J, Parish J, Atkins T, Asher A, Hadjipanayis CG, Burri SH, Green S, Olson JJ. Congress of Neurological Surgeons systematic review and evidence-based guidelines on the role of radiosurgery and radiation therapy in the management of patients with vestibular schwannomas. Neurosurgery. 2018 Feb 1;82(2):E49-51. PubMed

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

NEATS Assessment

National Guideline Clearinghouse (NGC) has assessed this guideline's adherence to standards of trustworthiness, derived from the Institute of Medicine's report Clinical Practice Guidelines We Can Trust.

= Poor = Fair = Good = Very Good = Excellent

Assessment	Standard of Trustworthiness
YES	Disclosure of Guideline Funding Source
	Disclosure and Management of Financial Conflict of Interests
	Guideline Development Group Composition
YES	Multidisciplinary Group

UNKNOWN	Methodologist Involvement
▮▯▯▯▯	Patient and Public Perspectives
	Use of a Systematic Review of Evidence
▮▮▮▮▮	Search Strategy
▮▮▮▮▮	Study Selection
▮▮▮▮▯	Synthesis of Evidence
	Evidence Foundations for and Rating Strength of Recommendations
▮▮▮▯▯	Grading the Quality or Strength of Evidence
▮▮▮▮▯	Benefits and Harms of Recommendations
▮▮▮▮▮	Evidence Summary Supporting Recommendations
▮▮▮▮▯	Rating the Strength of Recommendations
▮▮▮▮▮	Specific and Unambiguous Articulation of Recommendations
▮▯▯▯▯	External Review
▮▮▮▯▯	Updating

Recommendations

Major Recommendations

Definitions for the classification of evidence (I-III) and levels of recommendations (1-3) are provided at the end of the "Major Recommendations" field.

Please see the full-text version of this guideline (see the "Availability of Companion Documents" field) for the target population of each recommendation listed below.

Radiosurgery vs Observation

Question

What are the indications for stereotactic radiosurgery (SRS) treatment vs observation for patients with intracanalicular vestibular schwannomas without evidence of radiographic progression?

Recommendation

Level 3: If tinnitus is not observed at presentation, it is recommended that intracanalicular vestibular schwannomas and small tumors (<2 cm) without tinnitus be observed as observation does not have a negative impact on tumor growth or hearing preservation compared to treatment.

Radiosurgery Technology

Question

Is there a difference in outcome based on radiosurgery equipment used: Gamma Knife (Elekta, Stockholm, Sweden) vs linear accelerator-based radiosurgery vs proton beam?

Recommendation

There are no studies that compare 2 or all 3 modalities. Thus, recommendations on outcome based on modality cannot be made.

Radiosurgery Technique

Question

Is there a difference in outcome based on the dose delivered?

Recommendation

Level 3: As there is no difference in radiographic control using different doses, it is recommended that for single fraction SRS doses, <13 Gy be used to facilitate hearing preservation and minimize new onset or worsening of preexisting cranial nerve deficits.

Question

Is there a difference in outcome based on the number of fractions?

Recommendation

As there is no difference in radiographic control and clinical outcome using single or multiple fractions, no recommendations can be given.

Radiographic Follow-Up, Retreatment, and Tumorigenesis after Radiosurgery

Question

What is the best time sequence for follow-up images after SRS?

Recommendation

Level 3: Follow-up imaging should be obtained at intervals after SRS based on clinical indications, a patient's personal circumstances, or institutional protocols. Long-term follow-up with serial magnetic resonance images to evaluate for recurrence is recommended. No recommendations can be given regarding the interval of these studies.

Question

Is there a role for retreatment?

Recommendation

Level 3: When there has been progression of tumor after SRS, SRS can be safely and effectively performed as a retreatment.

Question

What is the risk of radiation-induced malignant transformation of vestibular schwannomas treated with SRS?

Recommendation

Level 3: Patients should be informed that there is minimal risk of malignant transformation of vestibular schwannomas after SRS.

Neurofibromatosis Type 2

Question

What are the indications for SRS in patients with neurofibromatosis type 2?

Recommendation

Level 3: Radiosurgery is a treatment option for patients with neurofibromatosis type 2 whose vestibular schwannomas are enlarging and/or causing hearing loss.

Definitions

American Association of Neurological Surgeons/Congress of Neurological Surgeons Classification of Evidence on Therapeutic Effectiveness

Evidence Classification	
Class I Evidence	Evidence provided by one or more well-designed randomized controlled clinical trials, including overview (meta-analyses) of such trials
Class II Evidence	Evidence provided by well-designed observational studies with concurrent controls (e.g., case-control and cohort studies)
Class III Evidence	Evidence provided by expert opinion, case series, case reports, and studies with historical controls

American Association of Neurological Surgeons/Congress of Neurological Surgeons Levels of Recommendation

Levels of Recommendation	
Level 1	Generally accepted principles for patient management, which reflect a high degree of clinical certainty (usually this requires class I evidence which directly addresses the clinical questions or overwhelming class II evidence when circumstances preclude randomized clinical trials)
Level 2	Recommendations for patient management which reflect clinical certainty (usually this requires class II evidence or a strong consensus of class III evidence)
Level 3	Other strategies for patient management for which the clinical utility is uncertain (inconclusive or conflicting evidence or opinion)

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Vestibular schwannomas

Guideline Category

Assessment of Therapeutic Effectiveness

Management

Clinical Specialty

Neurological Surgery

Neurology

Otolaryngology

Radiation Oncology

Radiology

Intended Users

Physicians

Guideline Objective(s)

- To summarize the role of stereotactic radiosurgery (SRS) on vestibular schwannoma (VS) tumor control, i.e., the lack of radiographic progression, its side effects, including new deficits and potential malignant transformation or tumorigenesis in patients with sporadic VSs and in patients with neurofibromatosis type 2 (NF2), using different delivery technologies and techniques
- To explore the necessary radiographic follow-up after SRS and the role of SRS for patients with VSs who show radiographic progression

Target Population

- Adults with vestibular schwannomas (VSs)
- Adults with VSs who have a diagnosis of neurofibromatosis type 2 (NF2)

Interventions and Practices Considered

1. Observation
2. Stereotactic radiosurgery (SRS)
3. Follow-up imaging
4. Retreatment using SRS

Major Outcomes Considered

- Tumor growth rates
- Hearing preservation rates
- Tumor control rates
- Progression-free survival
- Adverse effects of treatment

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Search Method

A broad search strategy was used because of the relatively small number of studies on each specific topic. PubMed and the Cochrane Library were searched according to the strategy summarized in Table 1 in the full guideline (see the "Availability of Companion Documents" field). The searches of electronic databases were supplemented with manual screening of the bibliographies of all retrieved publications. The bibliographies of recent systematic reviews and other review articles were also searched for potentially relevant citations. All articles identified were subject to the study selection criteria listed below. As noted above, the guideline committee also examined lists of included and excluded studies for errors and omissions. The task force went to great lengths to obtain a complete set of relevant articles. Having a complete set ensures that the guideline is not based on a biased subset of articles.

General Eligibility Criteria for Literature

General eligibility criteria were then applied with the resultant narrowing of the abstract publications as follows:

Deduplication of references
Limiting to human references
Limiting to English references
Limiting to January 1, 1946 to December 31, 2014

Article Inclusion and Exclusion Criteria

Abstracts for the initial 956 references were then reviewed and selected based on them meeting the following predetermined criteria:

General

Investigated patients suspected of having vestibular schwannomas (VSs)
Was of humans
Was not an in vitro study
Was not a biomechanical study
Was not performed on cadavers
Was published between January 1, 1990 and December 31, 2014
Was published in a peer-reviewed journal
Was not a meeting abstract, editorial, letter, or commentary
Was published in English
Was not a review article

Specific

Outcomes that included adult patients with VSs,
AND
Outcomes following radiation therapy reported in ≥5 patients

Figure 1 in the full guideline (PRISMA diagram) summarizes the flow after the literature search.

Search Strategies

The task force collaborated with a medical librarian to search for articles published between January 1, 1990 and December 31, 2014. Two electronic databases, PubMed and the Cochrane Library, were searched. Strategies for searching electronic databases were constructed by the evidence-based clinical practice guideline task force members and the medical librarian using previously published search strategies to identify relevant studies (see Table 1 and Figure 1 in the full guideline).

Number of Source Documents

One hundred and thirty-seven studies were included as evidence. See Figure 1 in the full guideline (see the "Availability of Companion Documents" field).

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

American Association of Neurological Surgeons/Congress of Neurological Surgeons Classification of Evidence on Therapeutic Effectiveness

Evidence Classification	
Class I Evidence	Evidence provided by one or more well-designed randomized controlled clinical trials, including overview (meta-analyses) of such trials
Class II Evidence	Evidence provided by well-designed observational studies with concurrent controls (e.g., case-control and cohort studies)
Class III Evidence	Evidence provided by expert opinion, case series, case reports, and studies with historical controls

Methods Used to Analyze the Evidence

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Study Selection, Quality Assessment, and Statistical Methods

Articles that met the eligibility criteria were grouped according to the questions they addressed and used to create the evidence tables and scientific foundation sections. Reasons for exclusion for papers were also documented to be able to discuss pertinent problem citations in the scientific foundation as needed.

Studies that met the eligibility criteria were subject to more detailed scrutiny and had their data extracted by 1 reviewer and the extracted information was checked by 1 or more other reviewers. Evidence and summary tables, reporting the extracted study information and evidence classification, were generated for all the included studies for each of the questions. Evidence tables were created with the most recent data first and subsequent listings in retrograde chronological order. The table headings consisted of first author name and year, followed by a brief study description, chosen data class, and conclusion. The authors were directed to craft the data in the tables in a succinct and fact-filled manner to allow for rapid understanding of the literature entry by the readership. The literature in the evidence tables was expanded upon in the Results section of each guideline article to emphasize important points supporting its classification and contribution to recommendations. The method by which this was accomplished is expanded upon in the Joint Guideline Committee (JGC) Guideline Development Methodology document (see the "Availability of Companion Documents" field).

Methods Used to Formulate the Recommendations

Expert Consensus (Nominal Group Technique)

Description of Methods Used to Formulate the Recommendations

Internal drafts of the tables and manuscripts were developed by sharing them between writers electronically, by telephone, and in face-to-face meetings. Summary and conclusion statements were included for each section, with comments on key issues for future investigation being added where pertinent.

Writing Group and Questions Establishment

After establishing vestibular schwannoma (VS) management as a priority for guideline development, the Joint Tumor Section of the American Association of Neurological Surgeons (AANS) and the Congress of Neurological Surgeons (CNS) and the Guidelines Committee of the Congress of Neurological Surgeons selected a multidisciplinary group of individuals to carry out this project. The entire group of individuals were screened for conflict of interest and then assembled into smaller groups by general components of management. These groups then agreed upon the main questions pertinent to these management components and shared them with the overall group for modification. The task force was divided into groups by management topic and proceeded with writing of the guidelines.

Classification of Evidence and Guideline Formulation

The concept of linking evidence to recommendations has been further formalized by the American Medical Association (AMA) and many specialty societies, including AANS, CNS, and the American Academy of Neurology (AAN). This formalization involves the designation of specific relationships between the strength of evidence and the strength of recommendations to avoid ambiguity. In the paradigm for therapeutic maneuvers, evidence is classified according to the scheme in the "Rating Scheme for the Strength of the Evidence" and "Rating Scheme for the Strength of the Recommendations" fields). A basis for these guidelines can be viewed in the Joint Guidelines Committee methodology document (see the "Availability of Companion Documents" field).

Guideline Panel Consensus

Multidisciplinary writing groups were created for each section based on author expertise to address each of the disciplines and particular areas of therapy selected for these clinical guidelines. Each group was involved with literature selection, creation and editing of the evidence tables, and scientific foundations for their specific section and discipline. Using this information, the writing groups then drafted the recommendations in answer to the questions formulated at the beginning of the process, culminating in the clinical practice guideline for their respective discipline. The draft guidelines were then circulated to the entire clinical guideline panel to allow for multidisciplinary feedback, discussion, and ultimately approval.

Rating Scheme for the Strength of the Recommendations

American Association of Neurological Surgeons/Congress of Neurological Surgeons Levels of Recommendation

Levels of Recommendation	
Level 1	Generally accepted principles for patient management, which reflect a high degree of clinical certainty (usually this requires class I evidence which directly addresses the clinical questions or overwhelming class II evidence when circumstances preclude randomized clinical trials)
Level 2	Recommendations for patient management which reflect clinical certainty (usually this requires class II evidence or a strong consensus of class III evidence)
Level 3	Other strategies for patient management for which the clinical utility is uncertain (inconclusive or conflicting evidence or opinion)

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

Internal Peer Review

Description of Method of Guideline Validation

Approval Process

The completed evidence-based clinical practice guidelines for the management of vestibular schwannomas (VSs) were presented to the Joint Guideline Committee (JGC) of the American Association of Neurological Surgeons (AANS) and the Congress of Neurological Surgeons (CNS) for review. The reviewers for the JGC were vetted by *Neurosurgery* for suitability and expertise to serve as reviewers for the purposes of publication in that journal also. The final product was then approved and endorsed by the executive committees of both the AANS and CNS before publication in *Neurosurgery*.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Only class III evidence studies are currently available to formulate these guidelines.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate use of radiosurgery and radiation therapy in management of vestibular schwannomas (VSs)

Potential Harms

Adverse effects of radiation, including decreased hearing, increased nerve deficits, hydrocephalus, and malignant transformation or tumorigenesis

Qualifying Statements

Qualifying Statements

Disclaimer of Liability

This clinical systematic review and evidence-based guideline was developed by a multidisciplinary physician volunteer task force and serves as an educational tool designed to provide an accurate review of the subject matter covered. These guidelines are disseminated with the understanding that the recommendations by the authors and consultants who have collaborated in their development are not

meant to replace the individualized care and treatment advice from a patient's physician(s). If medical advice or assistance is required, the services of a competent physician should be sought. The proposals contained in these guidelines may not be suitable for use in all circumstances. The choice to implement any particular recommendation contained in these guidelines must be made by a managing physician in light of the situation in each particular patient and on the basis of existing resources

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Quick Reference Guides/Physician Guides

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

IOM Domain

Effectiveness

Identifying Information and Availability

Bibliographic Source(s)

Germano IM, Sheehan J, Parish J, Atkins T, Asher A, Hadjipanayis CG, Burri SH, Green S, Olson JJ. Congress of Neurological Surgeons systematic review and evidence-based guidelines on the role of radiosurgery and radiation therapy in the management of patients with vestibular schwannomas. Neurosurgery. 2018 Feb 1;82(2):E49-51. PubMed

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2018 Feb 1

Guideline Developer(s)

Congress of Neurological Surgeons - Professional Association

Source(s) of Funding

These evidence-based clinical practice guidelines were funded exclusively by the Congress of Neurological Surgeons and the Tumor Section of the Congress of Neurological Surgeons and the American Association of Neurological Surgeons, which received no funding from outside commercial sources to support the development of this document.

Guideline Committee

Vestibular Schwannoma Evidence-Based Practice Guideline Task Force

Composition of Group That Authored the Guideline

Task Force Members: Isabelle M. Germano, MD, Department of Neurological Surgery, Icahn School of Medicine at Mount Sinai, New York, New York; Jason Sheehan, MD, PhD, Department of Neurological Surgery, University of Virginia, Charlottesville, Virginia; Johnathan Parish, MD, Carolinas Medical Center, Charlotte, North Carolina; Tyler Atkins, MD, Department of Neurosurgery and Spine, Carolinas Medical Center, Charlotte, North Carolina; Anthony Asher, MD, Carolina Neurosurgery and Spine Associates, Charlotte, North Carolina; Constantinos G. Hadjipanayis, MD, PhD, Department of Neurological Surgery, Icahn School of Medicine at Mount Sinai, New York, New York; Stuart H. Burri, MD, Department of Radiation Oncology, Levine Cancer Institute, Charlotte, North Carolina; Sheryl Green, MBBCh, Department of Radiation Oncology, Icahn School of Medicine at Mount Sinai, New York, New York; Jeffrey J. Olson, MD, Department of Neurosurgery, Emory University School of Medicine, Atlanta, Georgia

Financial Disclosures/Conflicts of Interest

Conflict of Interest

The Vestibular Schwannoma Guidelines Task Force members were required to report all possible conflicts of interest (COIs) prior to beginning work on the guideline, using the COI disclosure form of the American Association of Neurological Surgeons/Congress of Neurological Surgeons (AANS/CNS) Joint Guidelines Committee, including potential COIs that are unrelated to the topic of the guideline. The CNS Guidelines Committee and Guideline Task Force Chair reviewed the disclosures and either approved or disapproved the nomination. The CNS Guidelines Committee and Guideline Task Force Chair are given latitude to approve nominations of Task Force members with possible conflicts and address this by restricting the writing and reviewing privileges of that person to topics unrelated to the possible COIs. The conflict of interest findings are provided in detail in the full-text introduction and methods manuscript (see the "Availability of Companion Documents" field).

Guideline Endorser(s)

American Association of Neurological Surgeons - Medical Specialty Society

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Available from the Neurosurgery Web site .

Availability of Companion Documents

The following are available:

Congress of Neurological Surgeons systematic review and evidence-based guidelines on the role of radiosurgery and radiation therapy in the management of patients with vestibular schwannomas. Full guideline. Schaumburg (IL): Congress of Neurological Surgeons (CNS); 2017 Dec 22. 74 p. Available from the Congress of Neurological Surgeons (CNS) Web site .

Congress of Neurological Surgeons systematic review and evidence-based guidelines on the treatment of adults with vestibular schwannomas: introduction and methods. Schaumburg (IL): Congress of Neurological Surgeons (CNS); 2017 Dec 22. 28 p. Available from the CNS Web site .

Olson JJ, Kalkanis SN, Ryken TC. Congress of Neurological Surgeons systematic review and evidence-based guidelines on the treatment of adults with vestibular schwannomas: executive summary. Neurosurgery. 2018 Feb 1;82(2):129-34. Available from the Neurosurgery Web site .

Congress of Neurological Surgeons (CNS). Guideline development methodology: endorsed by the American Association of Neurological Surgeons (AANS), the Congress of Neurological Surgeons (CNS), and the AANS/CNS Joint Guideline Committee. Schaumburg (IL): Congress of Neurological Surgeons (CNS); 2012 Feb. 12 p. Available from the CNS Web site .

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI Institute on May 7, 2018. The information was verified by the guideline developer on June 4, 2018.

This NEATS assessment was completed by ECRI Institute on April 25, 2018. The information was verified by the guideline developer on June 4, 2018.

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